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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/375,609	08/17/1999	LAWRENCE A. RHEINS	DERM1100-1	5338

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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	**PAPER NUMBER**
1647	26

DATE MAILED: 05/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	28

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 3/17/03

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed in** accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 11-63, 64, 65, 70-72, 76-78, 80-83, 85-87, 149-163 is/are pending in the application.
Of the above, claim(s) 11-63 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 64, 65, 70-72, 76-78, 80-83, 85-87, 149-163 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 11-63, 64, 65, 70-72, 76-78, 80-83, 85-87, 149-163 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

★ U.S. GPO: 1998-404-

Part III: Detailed Office Action

In the response filed 3/24/03, paper number 27, applicants argue the renumbering of claim 156 as 149, stating that claims 149-155 were added with the Supplemental Amendment filed 7/22/02. Noting that the Examiner in charge of the case at that time is no longer at the USPTO, the Examiner finds that the file-wrapper indeed indicates the presence of such claims at that date, however no corresponding amendment exists. In the interest of a complete prosecution history, applicants are required to provide, with their response to this Office Action, a copy of said paper. In view of this situation, the Examiner accepts applicants presentation of all claims currently under consideration in paper number 27, which presentation is accepted as an accurate and complete copy of all claims currently under consideration.

Claims 64, 65, 70-72, 76-78, 80-83, 85-87 and 149-163, *as presented in paper number 27*, are under consideration.

Claims 11-63 remain withdrawn from prosecution, election having been made without traverse in paper number 6, filed 11/17/00.

Double Patenting Rejections:

Applicants statement that no action regarding potential double patenting among the numerous copending applications is currently necessary it noted. Applicants are reminded to take appropriate action, and requested to inform the Examiner, should the situation change.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 65, 149-156 and 163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention.

Claims 65 and 161 appear to be duplicative, and are therefore indefinite; it is not clear how the sample could comprise cells "associated" with the stratum corneum, as recited in claim 161, without also comprising stratum corneum cells themselves, as recited in claim 65.

Claim 149 recites that the adhesive tape is removed from the skin "such that a sample comprising" a RNA is obtained, and dependent claims 151 and 153 further state that the tape is applied and removed such that the sample comprises mRNA, and RNA encoding a cytokine, respectively. The Examiner interprets the recitation "such that" no differently from the formerly used language, "in a manner such that". Accordingly, the claims are indefinite, as no method steps are recited that would specifically result in the recited outcome. Tape stripping may or may not result in the isolation of the recited compounds, however there are no particular method steps disclosed that would accomplish said specifically recited outcomes. Amendment of the claims to indicate that it is RNA, mRNA or RNA encoding a cytokine (respectively) that is to be *isolated or detected*, as opposed to obtained, would be remedial.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 71, 156, 159 and 160 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As stated in the previous Office action, there appears to be no basis for stripping the skin 1-2 times. Applicants have pointed to page 3, lines 14-15 for basis for such, however the specification

merely states "1 or more times" at that location. Accordingly, while there is basis for stripping 1 time, 1 or more times, or 1-25 times, there does not appear to have been contemplation of specifically 1-2 times at the time the invention was made, and therefore claims 71 and 156 comprise new matter.

With regard to claims 159-160, which contain the newly introduced limitation that the skin is contacted with "an external agent that causes dermatitis before applying the adhesive tape" and wherein that agent is SLS, applicants point to page 2 lines 10-11 and Example 2 for support for that limitation. This has been fully considered but is not persuasive. The specification at page 2 merely states that a broad array of agents may cause inflammation or contact dermatitis, not that the invention is directed to a method which *comprises causing* such dermatitis. Similarly, Example 2 uses a test system in which contact dermatitis case induced using SLS for the purpose of detecting changes in cytokine expression in the affected skin. However, there is no disclosure that *causing* such dermatitis is part of the invention, nor does the specification give any reason for doing so. Accordingly, the newly introduced method steps constitute new matter.

Claim 82 remains rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for detection of nucleic acids encoding leukotriene or prostaglandin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Neither substance is encoded by nucleic acids. While applicants have cancelled these species from other claims, they remain in claim 82.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 64, 65, 76, 85, 86, and 161-162 are rejected under 35 U.S.C. 102(b) as anticipated, and Claim 70 is rejected under(b) as anticipated by or in the alternative under 35 U.S.C. 103(a) as obvious over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996.

Garofano et al. obtained skin cell samples by "pressing many times the adhesive tapes on the collecting surface (perioral, wrist, back of hand, or finger) until the adhesive power was lost. DNA was then extracted from the samples, and amplified and identified via PCR. Although Garofano et al. are silent with respect to cell types obtained, the samples would necessarily have contained stratum corneum and associated cells, as claimed. Accordingly, claims 64, 65, 76, 85, 86, and 161-162 are anticipated by Garofano et al.

With respect to claim 70, the Examiner is unable to determine exactly how many times the tape was pressed to the skin before the adhesive power was lost; it seems likely that it was less than 25, but no determination can be made. Under such circumstances, where the product seems to be identical, then the burden shifts to applicant to provide evidence that the prior art would neither

anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Claims 71-72, are rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996.

The teachings of Garofano et al. are summarized above. Claims 70-72 introduced limitations that the tape is applied a specific number of times. It would have been obvious to the person of ordinary skill in the art to determine the minimum number of applications of tape required to obtain a sufficient sample size. The skilled artisan would have been motivated to do so to minimize stress and trauma on the patient, both well-recognized motivations in the medical arts. Accordingly, the invention, taken as a whole, is *prima facie* obvious over Garofano et al.

Claims 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view of applicants admissions of the prior art.

The teachings of Garofano et al. are summarized above. Claims 80-82 differ from the reference in that different DNAs were detected by Garofano than are recited in the claims. However, given Garofano's demonstration of the presence of nucleated cells in the sample, and the ability to amplify the desired nucleic acids with PCR, it would have been obvious to the person of ordinary skill in the art at the time the invention was made that Garofano's method could be used for the detection of any desired DNA, and especially IL-1, -3, -4, -6, -7, -8, -10, -12 or GM-CSF, in view of applicants admission that it was known in the prior art at the time the invention was made that keratinocytes express those cytokines. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

Claims 77-78, 80-83, 149-154 ,156-158 and 163 are rejected under 35 U.S.C. 103(a) as being

unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view Paludan et al., J. Invest. Derm. 99:830-835, 1992, previously of record.

The rejected Claims differ from the teachings of Garofano et al. in that they require isolation or detection of RNA, including mRNA.

Paludan et al. disclose assaying for IL-8 mRNA levels on samples obtained by skin scraping. They state "Our technique has proved useful for discriminating between epidermal IL-8 mRNA levels in a variety of inflammatory skin diseases and reactions, and should be applicable to analysis of other cytokine mRNAs and other skin compartments."

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the method disclosed by Garofano et al. to detect mRNA of cytokines as taught by Paludan et al. The person of ordinary skill in the art would have been motivated to make the substitution in view of the less invasive nature of Garofano's methods, and would have expected success, as Garofano et al. specifically disclose that nucleated cells were obtained. The person of ordinary skill in the art would recognize that nucleated cells would be expected to contain RNA, including mRNA, as detected by Paludan et al. Further, in view of Paludan's teachings, it would have been obvious to use the method of Garofano et al. to detect samples from individuals with inflammatory skin diseases and/or reactions. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

Claim 155 rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view Paludan et al., J. Invest. Derm. 99:830-835, 1992, previously of record as cited in the rejection of claims is 77-78, 80-83, 149-154 ,156-158 and 163 above, and further in view of Ramsay et al., U.S. Patent Number 6,056,859 and Furcht et al., U.S. Patent Number 6,054,277, both previously of record.

Claim 155 recites that the RNA is detected using a DNA array. Ramsay et al. and Furcht et al. both teach the use of chips, or DNA arrays, for nucleic acid sequence analysis. The stated benefits of the technologies are speed and reduced cost. It would have been obvious to the person

of ordinary skill in the art at the time the intention was made to modify the method found obvious over Garofano et al. and Paludan et al., above, to include analysis using DNA arrays as taught by Ramsey et al. and Furcht et al. for the purpose of attaining the known and expected benefits of the chip technology. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

Claim 87 is rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view of Frayne, U.S. Patent Number 5,811,239, previously of record.

Claim 87 recites that the identifying or quantifying is by hybridization with a polynucleotide probe.

Frayne teaches that it was well known in the art to detect DNA sequence variation for the purpose of identifying genetic disease, genetic linkage studies, identity determination, etc. She further teaches that PCR, hybridization and RNase protection are well known techniques for doing so, see paragraph bridging columns 1-2.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the isolation method of Garofano et al. to obtain samples to be used in the detection methods taught as being routine in the art by Frayne. The person of ordinary skill in the art would have been motivated to do so to attain the known advantages of ease or isolation of cells as taught by Garofano et al. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

Advisory Information:

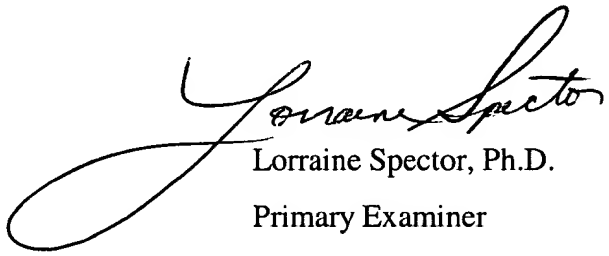
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 5:00 A.M. to 9:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, can be reached at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Examiner Spector via telephone number 703-746-5228. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.



Lorraine Spector, Ph.D.
Primary Examiner